REMARKS

I. Amendments

Claims 12, 21, 23 and 25 have been amended. Claims 16, 20, 22, 24 and 26-30 have been canceled. The newly added claims do not constitute new matter and are completely supported throughout the specification and originally filed claims. More particularly, the amendments to the claims may be found, for example, at page 4, lines 25-27, page 5, lines 6-13, page 8, lines 21-22, page 12, line 28 through page 16, line 31 and page 53, lines 8-14 of the specification.

The foregoing amendments are made solely to place the claims in condition for allowance, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 12, 21, 23 and 25 are pending in the instant application.

II. Rejections

A. *Rejection under 35 U.S.C. § 112*

1) The Examiner has rejected claims 12 and 21-30 under 35 U.S.C. § 112, first paragraph, because they allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 12 and 21-30 are drawn to a transgenic mouse comprising a disruption in the NPY6 receptor gene, wherein where the disruption is homozygous, the transgenic mouse exhibits a neuromuscular phenotype. According to the Examiner, the specification does not support the limitation of a "neuromuscular phenotype," but only supports the phenotype of increased agility or coordination.

The Applicant respectfully traverses the rejection. However, in order to place the claims in condition for allowance, the Applicant has amended the claims, rendering the rejection moot. Pending claims 12, 21, 23 and 25 as amended recite a transgenic mouse exhibiting a phenotype

of increased agility or coordination, which are described in the specification in such a way as to meet the written description requirements set forth in 35 U.S.C. § 112, first paragraph.

2) The Examiner has also rejected claim 24 under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

According to the Examiner, claim 24, drawn to a cell isolated from a transgenic mouse having a disruption of the NPY6 receptor gene, wherein where the disruption is homozygous the mouse exhibits the phenotype of increased agility or coordination, is not supported by the specification because the specification fails to teach how to use a cell isolated from the transgenic mouse. In particular, the Examiner asserts that, although the specification has disclosed a use for transgenic mouse of screening agents that ameliorate the phenotype of increased agility or coordination, the specification allegedly does not disclose any use applicable to the cells.

The Applicant respectfully traverses the rejection. The Applicant believes one skilled in the art would be able to use the cells of the present invention without undue experimentation. As one example, the cells may be used to determine whether potential agents can recover the disrupted NPY6 receptor, such as, for example, by upregulating the expression of the disrupted NPY6 receptor gene and/or recovering the decreased activity from the disruption. As another example, the cells may be used in secondary assays to screen hit compound demonstrated to be capable to affect coordination or agility in order to determine other effects of the hit compounds. These uses of the recited cells would be well within the knowledge of the skilled artisan. In any case, the Applicant has cancelled claim 24 in order to place the claims in condition for allowance. Therefore, the rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant.

As the rejections of the claims under 35 U.S.C. § 112, first paragraph, are no longer relevant, Applicant respectfully requests withdrawal of the rejections. Applicant submits that claims 12, 21, 23 and 25 as amended are patentable and meet the requirements of 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 103

Claims 26-30 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Mansour *et al.*, 1988, *Nature,* 336(24): 348-352 ("Mansour") in view of Weinberg *et al.,* 1996, *J*

Biol Chem, 271(28): 16435-16438 ("Weinberg"). Applicants respectfully traverse this rejection. The Applicant respectfully traverses this rejection.

As noted, Mansour describes a general approach for isolating embryonic stem cells containing a targeted mutation in a gene, provided that a cloned fragment of the gene is available. More particularly, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int*-2 in mouse embryo-derived stem cells by homologous recombination using targeting constructs pRV9.1/TK and pINT-2-N/TK, respectively. The Examiner has conceded in the Office Action mailed September 9, 2002 that Mansour does not teach how to make an NPY6 receptor targeting construct and knockout mouse.

Weinberg merely teaches the identification and cloning of a NPY6 gene. Clearly, Weinberg lacks any disclosure related to disrupting the NPY6 gene in the mouse using a targeting construct as recited in the pending claims.

Claims 26-30 are drawn to a targeting vector capable of disrupting NPY6 receptor gene, wherein when the targeting vector is introduced into a murine embryonic stem cell, results in a transgenic mouse comprising a disruption in the NPY6 receptor gene exhibiting increased agility or coordination, and to methods of creating the targeting vector and cells transformed with the targeting vector.

As a basis of the obviousness rejection under 35 U.S.C. § 103, the Examiner argues that because the claims recite the phenotype of the transgenic mouse in such a way as to merely define the use of the targeting vector recited in these claims, the ordinary artisan would have been motivated to knock out the expression of the NPY6 gene in a mouse to study the role it plays in the complex biology of NPY and determine which NPY signaling pathway(s) it mediates, as suggested by Weinberg. The Examiner further asserts that the ordinary artisan would have had a reasonable expectation of success because of the teachings of Mansour and Weinberg. The Applicant respectfully disagrees.

The Applicant maintains his arguments set forth in the Response filed March 10, 2003, that suggestions by Weinberg that the NPY6 receptor is involved in various biological functions and that the development of antisense oligonucleotides or NPY6-specific antibodies would help address the precise physiological role of the NPY6 receptor is not sufficient motivation to modify Weinberg or to combine Weinberg with Mansour to produce an NPY6 gene targeting vector used to knockout NPY6 receptor gene in a mouse. The Applicant maintains that

Weinberg does not, in any way, suggest the desirability of creating a targeting vector in order to disrupt the NPY6 gene, even as a way to further elucidate the physiological role of the receptor. The mere fact that a reference can be modified does not render the invention obvious unless the prior art also suggests the desirability of the modification.

The Examiner has also maintained the argument that the ordinary artisan would have had a reasonable expectation of success because of the teachings of Mansour, who teaches a general method of targeted gene disruption in mice based on homologous recombination using a cloned fragment of a desired gene. However, the Applicant contends that the Examiner has failed to show any teaching, motivation or suggestion to combine the references. The mere fact that the references can be combined does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. Further, the fact that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. Finally, the level of skill in the art cannot be relied upon to provide the suggestion to combine references. In the instant case, there is no motivation to combine the teachings of Mansour with Weinberg to achieve the claimed invention. Mansour teaches a general method of targeted gene disruption in mice based on homologous recombination using a cloned fragment of a gene. There is no teaching or suggestion in Mansour as to the desirability of using a targeting vector as claimed to create a targeted disruption of a NPY6 receptor gene. Similarly, Weinberg teaches the coding sequence of the NPY6 gene, but contains no suggestion to create a targeted disruption of an NPY6 gene using the targeting vector as recited in the pending claims.

Finally, the Applicant maintains that neither Mansour nor Weinberg, alone or in combination, teaches all of the limitations of the instant claims. For example, neither Mansour nor Weinberg teach or suggest a targeting vector capable of disrupting a NPY6 receptor gene in a cell, and using the cell to create a transgenic mouse with a disrupted NPY6 gene exhibiting a specific phenotype, particularly not increased agility or coordination, which invention is the subject of the pending claims.

Although the Applicant believes that claims 26-30 are not obvious in view of the sole or combined teachings of Mansour or Weinberg for the reasons set forth above, these claims have been canceled in order to place the claims in condition for allowance. In light of the cancellation

of claims 26-30, the rejection is no longer relevant, and Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-639.

Respectfully submitted,

Date: 9/3/03

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